STN- structure Search 2/9/06

10/801,069

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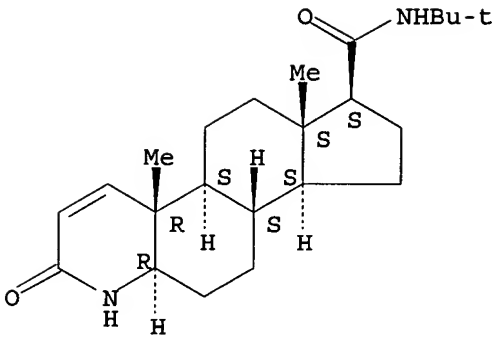
L4 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:531558 CAPLUS
DOCUMENT NUMBER: 143:261731
TITLE: GABRA2 alleles moderate the subjective effects of alcohol, which are attenuated by finasteride
AUTHOR(S): Pierucci-Lagha, Amira; Covault, Jonathan; Feinn, Richard; Nellissery, Maggie; Hernandez-Avila, Carlos; Oncken, Cheryl; Morrow, A. Leslie; Kranzler, Henry R.
CORPORATE SOURCE: Department of Psychiatry, Alcohol Research Center, University of Connecticut School of Medicine, Farmington, CT, USA
SOURCE: Neuropsychopharmacology (2005), 30(6), 1193-1203
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GABAA receptors are involved in the subjective effects of alc. Endogenous neuroactive steroids interact with GABAA receptors to mediate several behavioral effects of alc. in rodents. Based on a haplotypic association of alc. dependence with the gene encoding the GABAA receptor α-2 subunit (GABRA2), the authors examined whether GABRA2 alleles are associated with the subjective response to alc. The authors also examined whether finasteride (a 5-α steroid reductase inhibitor), which blocks the synthesis of some neuroactive steroids, reduces the subjective response to alc. In all, 27 healthy social drinkers (15 males) completed a randomized, double-blind, placebo-controlled study of high-dose finasteride. After being pretreated with study drug, subjects consumed three alc. drinks. Subjective effects were measured repeatedly over the ascending blood alc. curve. To examine the moderating role of genetic variation in GABRA2, a single-nucleotide **polymorphism** that was informative in association studies was included as a factor in the anal. Subjects homozygous for the more common A-allele (n = 7) showed more subjective effects of alc. than did individuals with one or two copies of the alc. dependence-associated G-allele (n = 20, including two homozygotes). Among the A-allele homozygotes, there was a greater reduction in several subjective effects during the finasteride session compared to the placebo session. These findings provide preliminary evidence that the risk of alcoholism associated with GABRA2 alleles may be related to differences in the subjective response to alc. The effects of finasteride provide indirect evidence for a mediating role of neuroactive steroids in some of the subjective effects of alc.
IT **98319-26-7**, Finasteride
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GABRA2 alleles moderate the subjective effects of alc., which are attenuated by finasteride)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:799595 CAPLUS
DOCUMENT NUMBER: 141:282839
TITLE: Novel crystalline forms of finasteride
INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari; Subash, Chander Reddy Kesireddy
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083230	A1	20040930	WO 2003-IN60	20030319

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

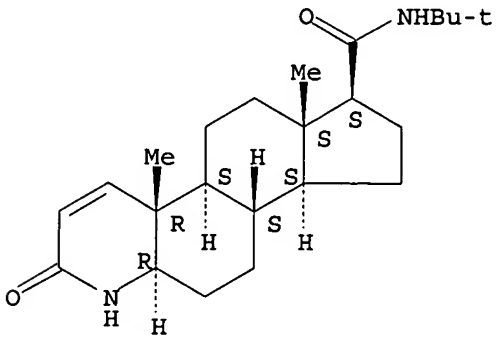
PRIORITY APPLN. INFO.: WO 2003-IN60 20030319

AB The present invention relates to novel crystalline forms of finasteride, to processes for their preparation and pharmaceutical compns. containing them. A process for preparation of finasteride crystalline forms comprises the steps of (i) dissolving finasteride in a solvent, e.g., an alc. or dioxane, (ii) maintaining the solution at certain elevated temperature (iii) cooling the solution slowly, (iv) maintaining the solution at lower temperature for certain time, and (v) filtering the solid separated For example, 10 g of finasteride was dissolved in 25 mL of methanol, heated to 55° and maintained at this temperature for 15 min. The solution was slowly cooled to 0° in 3 h and maintained at 0° for 1.5 h. The separated crystals were filtered at 0° to give 8.5 g of Form H1 of finasteride.

IT **98319-26-7**, Finasteride
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP

(Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of stable crystalline forms of finasteride for delivery systems)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:390268 CAPLUS
DOCUMENT NUMBER: 140:395528
TITLE: Method of obtaining **polymorphic** form I of finasteride
INVENTOR(S): Silva Guisasola, Luis Octavio; Laderas Munoz, Mario; Martin Juarez, Jorge
PATENT ASSIGNEE(S): Ragactives, S.L., Spain
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039828	A1	20040513	WO 2003-ES556	20031029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2206065	A1	20040501	ES 2002-2512	20021031
ES 2206065	B1	20050816		
EP 1580194	A1	20050928	EP 2003-769508	20031029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005228008	A1	20051013	US 2005-119027	20050429
PRIORITY APPLN. INFO.:			ES 2002-2512 A	20021031

WO 2003-ES556 W 20031029

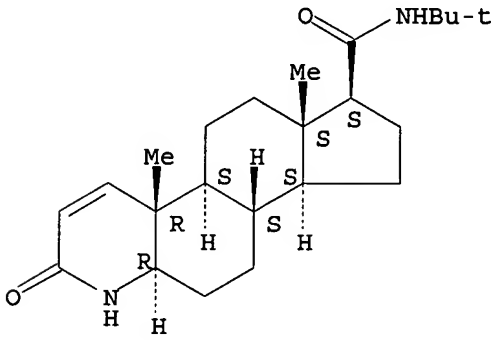
AB The invention relates to a method of obtaining **polymorphic** Form I of finasteride. The inventive method comprises the following steps: (i) finasteride is dissolved in a substantially-anhydrous organic solvent, which is selected from Bu acetate, iso-Bu acetate, sec-Bu acetate, tert-Bu acetate, alkyl acetate C5 and mixts. thereof, at a temperature which is equal to or less than the b.p. of the aforementioned organic solvent; (ii) the dissoln. of finasteride is cooled slowly to a cooling temperature which is determined according to the selected solvent; (iii) the resulting suspension is maintained at the cooling temperature for a period of, or less than, 16 h; and (iv) the solid phase containing crystals of Form I of finasteride is recovered, for example, by means of filtration and the solvent is removed, for example, by drying said crystals. The method can be used to obtain Form I of finasteride in the unique, pure form.

IT **98319-26-7P**, Finasteride
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(method of obtaining **polymorphic** form I of finasteride)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:249429 CAPLUS

DOCUMENT NUMBER: 139:67200

TITLE: Analysis of genetic **polymorphisms** of steroid 5α-reductase type 1 and 2 genes in Korean men with androgenetic alopecia

AUTHOR(S): Ha, Seog-Jun; Kim, Jung-Soo; Myung, Jae-Wook; Lee, Hyun-Jeong; Kim, Jin-Wou

CORPORATE SOURCE: St. Paul's Hospital, Department of Dermatology, The Catholic University of Korea, Seoul, 130-709, S. Korea

SOURCE: Journal of Dermatological Science (2003), 31(2), 135-141
CODEN: JDSCEI; ISSN: 0923-1811

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Genetic **polymorphisms** of steroid 5α-reductase have been studied in androgenetic alopecia in Caucasians, but the genes encoding the two isoenzymes were not associated with male pattern baldness.

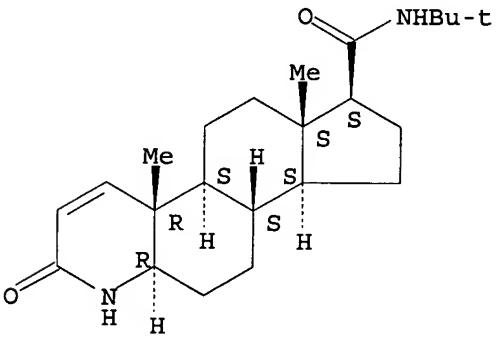
Genetic **polymorphisms** and ethnic variations have not been studied for Asians, although it is suggested that racial difference could exist and influence clin. phenotypes. Objective: The purpose of our study is to investigate the genetic **polymorphisms** of steroid 5α-reductase type 1 and 2 (SRD5A1 and SRD5A2) genes in Korean population, and to study the association of these **polymorphisms** with the development, clin. types (female or male pattern) and therapeutic response of androgenetic alopecia. Methods: Sixty-six patients with androgenetic alopecia and controls consisted of 92 healthy men were included. Twenty-four patients were treated with finasteride for at least 6 mo, and clin. responses were assessed by a simple classification. For type 1 isoenzyme, HinfI and NspI restriction fragment length **polymorphisms** (RFLPs) were detected using polymerase chain reaction method. For type 2 isoenzyme, RsaI RFLPs detected valine/leucine **polymorphisms** at codon 89, and MowI RFLPs detected alanine/threonine **polymorphisms** at codon 49. Results: We could not find any significant assocns. of the genetic **polymorphisms** of these two isoenzyme genes with androgenetic alopecia in Koreans (P>0.05). These **polymorphisms** were not associated with the clin. types of baldness or the response to finasteride (P>0.05). Conclusion: These results suggest that **polymorphisms** of SRD5A1 and SRD5A2 genes may not be directly associated with the development of baldness or generation of different clin. phenotypes.

IT **98319-26-7**, Finasteride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroid 5α-reductase type 1 and 2 genetic **polymorphisms** in Korean men with androgenetic alopecia)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:859280 CAPLUS

DOCUMENT NUMBER: 139:312088

TITLE: A spectroscopic and crystallographic study of **polymorphism** in an aza-steroid. [Erratum to document cited in CA134:32861]

AUTHOR(S): Wenslow, Robert M.; Baum, Mary W.; Ball, Richard G.; McCauley, James A.; Varsolona, Richard J.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0900, USA

SOURCE: Journal of Pharmaceutical Sciences (2002), 91(11), 2465

CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

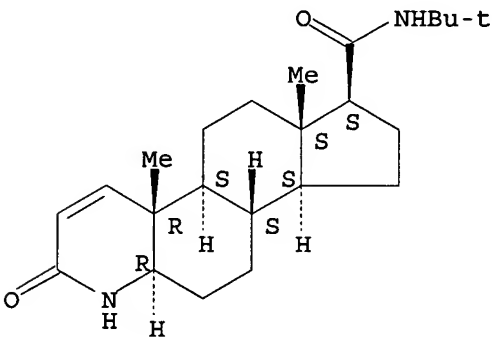
AB The solubility anal. in the exptl. section is incorrect. While the information about solubility trends and form stability are correct, the actual solubility values are unreliable. The solubility measurements portion of the exptl. section (page 1271), Figure 3 (page 1273), and the second paragraph of the results and discussion section (page 1272) must be retracted.

IT **98319-26-7**, Finasteride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spectroscopic and crystallog. study of **polymorphism** in aza-steroid (Erratum))

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:340897 CAPLUS
DOCUMENT NUMBER: 137:232803

TITLE: 13C-NMR study of 4-azasteroids in solution and solid state

AUTHOR(S): Morzycki, Jacek W.; Wawer, Iwona; Gryszkiewicz, Agnieszka; Maj, Jadwiga; Siergiejczyk, Leszek; Zaworska, Alicja
CORPORATE SOURCE: Institute of Chemistry, University of Bialystok, Bialystok, 15-443, Pol.

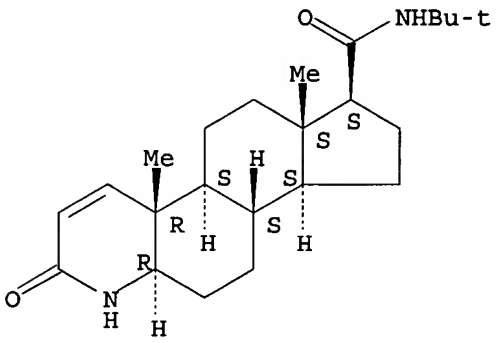
SOURCE: Steroids (2002), 67(7), 621-626
CODEN: STEDAM; ISSN: 0039-128X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A group of biol. active 4-azasteroids was studied by 13C-NMR spectroscopy in solution and in the solid phase. A full assignment of signals in the spectra of samples in chloroform was performed for thirteen 4-azasteroids using two-dimensional techniques. Substituent and steric effects of a nitrogen atom, and their influence on chemical shifts of the neighboring carbon atoms are discussed. CP MAS spectra were obtained for five 4-azasteroids including finasteride. The spectra confirmed **polymorphism** of the latter compound In addition to the **polymorphic** forms that are already known, a new mol. complex of finasteride with dioxane is reported.

IT **98319-26-7**

RL: PRP (Properties)
(13C-NMR study of 4-azasteroids in solution and solid state and identification of **polymorphism**)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:185148 CAPLUS
DOCUMENT NUMBER: 136:236864
TITLE: Preparation of **polymorphic** forms of 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-en-3-one (finasteride)
INVENTOR(S): Reddy, M. Satyanarayana; Rajan, S. T.; Rao, M. V. N. Brahmeshwara; Vyas, K.; Reddy, S. Vishnuvardhana; Rekha, K. Shashi
PATENT ASSIGNEE(S): Reddy's Laboratories Ltd., India; Cord, Janet I.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020553	A1	20020314	WO 2001-US19546	20010619
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2422159	AA	20020314	CA 2001-2422159	20010619
AU 2001069911	A5	20020322	AU 2001-69911	20010619
EP 1322663	A1	20030702	EP 2001-948467	20010619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013732	A	20030729	BR 2001-13732	20010619
JP 2004508380	T2	20040318	JP 2002-525173	20010619

NZ 525116	A	20041126	NZ 2001-525116		20010619
NO 2003001045	A	20030429	NO 2003-1045		20030306
ZA 2003002554	A	20040219	ZA 2003-2554		20030401
US 2005059691	A1	20050317	US 2004-801069		20040315
PRIORITY APPLN. INFO.:			IN 2000-DE737	A	20000907
			WO 2001-US19546	W	20010619

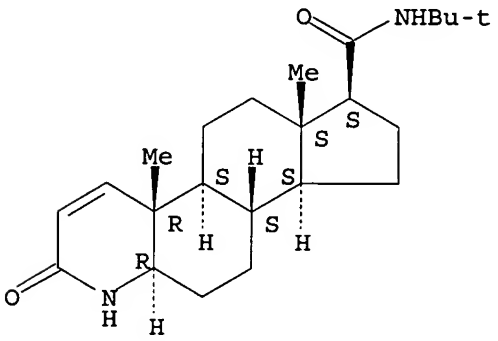
AB The present invention relates to a novel **polymorphic** form of 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-en-3-one (finasteride) and processes for preparing the **polymorph.** Thus, 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androstan-3-one was treated with 2,3-dichloro-5,6 dicyano benzoquinone and bis(trimethylsilyl)trifluoroacetamide in toluene medium at 80-110°. The toluene was removed to yield a solid that is crude finasteride. This compound was dissolved in CH2Cl2 saturated with petroleum ether. After removal of the solvents, the solid was dried to give the form III of finasteride.

IT **98319-26-7P**, Finasteride
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **polymorphic** forms of finasteride)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

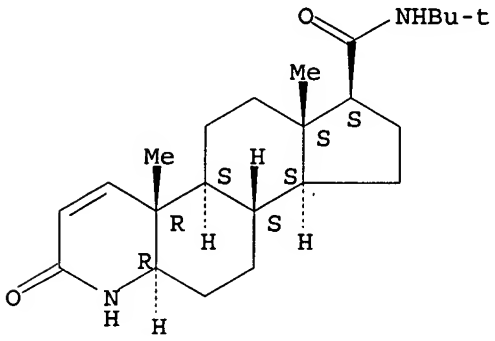
L4 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2000:737606 CAPLUS
DOCUMENT NUMBER:	134:32861
TITLE:	A spectroscopic and crystallographic study of **polymorphism** in an aza-steroid
AUTHOR(S):	Wenslow, Robert M.; Baum, Mary W.; Ball, Richard G.; Mccauley, James A.; Varsolona, Richard J.
CORPORATE SOURCE:	Merck Research Laboratories, Rahway, NJ, 07065-0900, USA
SOURCE:	Journal of Pharmaceutical Sciences (2000), 89(10), 1271-1285 CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER:	Wiley-Liss, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The crystal structures of 2 enantiotropic **polymorphs** of the aza-steroid, finasteride, were determined The solid-state NMR spectra, IR spectra, and phys. property data of these 2 **polymorphs** are discussed in relation to both their solid-state structures and hydrogen-bonding networks.

IT **98319-26-7**, Finasteride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spectroscopic and crystallog. study of **polymorphism** in aza-steroid)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:528014 CAPLUS
DOCUMENT NUMBER: 133:346313
TITLE: Biochemical and pharmacogenetic dissection of human steroid 5α-reductase type II
AUTHOR(S): Makridakis, Nick M.; di Salle, Enrico; Reichardt, Juergen K. V.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, and, Institute for Genetic Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA
SOURCE: Pharmacogenetics (2000), 10(5), 407-413
CODEN: PHMCEE; ISSN: 0960-314X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human prostatic steroid 5α-reductase, encoded by the SRD5A2 gene on chromosome band 2p23, catalyzes the irreversible conversion of testosterone to dihydrotestosterone (DHT), the most active androgen in the prostate, with NADPH as its cofactor. This enzyme has never been purified but a number of competitive inhibitors have been developed for this enzyme since increased steroid 5α-reductase activity may cause benign prostatic hypertrophy and prostate cancer. We report here the detailed biochem. and pharmacogenetic dissection of the human enzyme by analyzing 10 missense substitutions and three double mutants which are all naturally found in humans. Nine of these 13 mutants reduce activity (measured as Vmax) by 20% or more, three increase steroid 5α-reductase by more than 15% and one results in essentially unaltered kinetic properties suggesting that it is a truly neutral ("**polymorphic**") amino acid substitution. Substantial pharmacogenetic variation among the mutants was also observed when three competitive inhibitors, finasteride, GG745 (dutastcride) and PNU157706, were investigated. Our studies not only define the substrate and cofactor binding sites of human steroid 5α-reductase, but also have significant consequences for the

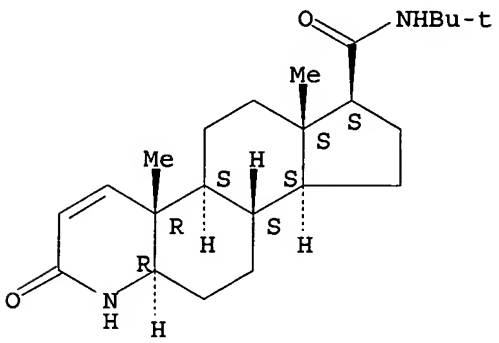
pharmacol. usage of steroid 5α-reductase inhibitors in human patients treated for prostatic conditions.

IT **98319-26-7**, Finasteride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biochem. and pharmacogenetic dissection of human steroid 5α-reductase type II)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:151800 CAPLUS
DOCUMENT NUMBER: 132:166387
TITLE: Finasteride preparation
INVENTOR(S): Slemon, Clarke
PATENT ASSIGNEE(S): Torcan Chemical Ltd., Can.
SOURCE: Brit. UK Pat. Appl., 14 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2338234	A1	19991215	GB 1998-12454	19980610
GB 2338234	B2	20000503		
CA 2389666	AA	20010510	CA 1999-2389666	19991101
WO 2001032683	A1	20010510	WO 1999-CA1017	19991101
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228084	A1	20020807	EP 1999-953456	19991101
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003513103	T2	20030408	JP 2001-535382	19991101

AU 773067	B2	20040513	AU 2000-10213		19991101
NO 2002002093	A	20020603	NO 2002-2093		20020502
ZA 2002004299	A	20030529	ZA 2002-4299		20020529
US 6677453	B1	20040113	US 2002-111979		20020618
PRIORITY APPLN. INFO.:			GB 1998-12454	A	19980610
			WO 1999-CA1017	W	19991101

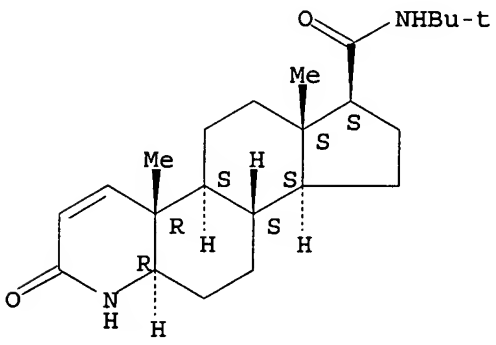
AB **Polymorphic** form I of finasteride was prepared by forming an insol. complex of finasteride and a Group I or Group II metal salt and the dissociating the complex by dissolving away the salt component with water to leave the substantially pure form I **polymorphic** crystalline finasteride.

IT **98319-26-7P**, Finasteride
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(finasteride preparation)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1999:127777 CAPLUS
DOCUMENT NUMBER:	130:282217
TITLE:	Structural characterization of **polymorphs** and molecular complexes of finasteride
AUTHOR(S):	Wawrzycka, Irena; Stepniak, Krystyna; Matyjaszczyk, Slawomir; Koziol, Anna E.; Lis, Tadeusz; Abboud, Khalil A.
CORPORATE SOURCE:	Fac. Chem., Maria Curie-Sklodowska Univ., Lublin, 20-031, Pol.
SOURCE:	Journal of Molecular Structure (1999), 474, 157-166 CODEN: JMOSB4; ISSN: 0022-2860
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The mol. structure of finasteride, 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-en-3-one, and structures of three related crystalline forms have been determined by X-ray anal. The rigid steroid skeleton of the mol. adopts a half-chair/chair/chair/half-chair conformation. Two peptide groups, one cyclic (lactam) in the ring A and a second being a part of the substituent at C17, are the main factors influencing intermol. contacts. Different hydrogen-bond interactions of these hydrophilic groups are observed in the crystal structures. An infinite ribbon of finasteride mols. is formed between lactam groups in the orthorhombic homomol. crystal obtained from an ethanol solution The linear mol. complex finasteride-acetic acid is connected by hydrogen bonds between the lactam of finasteride and the

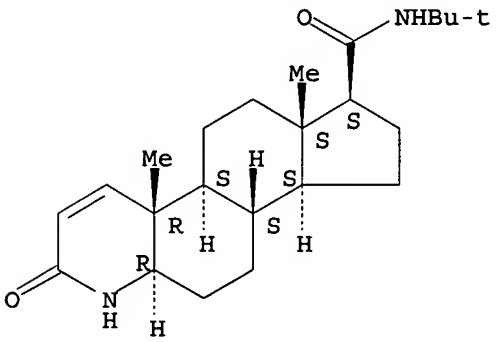
carboxyl group of acetic acid. The crystallization from an Et acetate solution gives
a complex structure of bis-finasteride monohydrate Et acetate clathrate with guest mol. disordered in channels. Crystals of a second (monoclinic) finasteride **polymorph** were obtained during thermal decomposition and sublimation. Two **polymorphic** forms show different IR spectra.

IT **98319-26-7**, Finasteride
RL: PRP (Properties)
(crystal structure; structural characterization of **polymorphs** and mol. complexes of finasteride)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:513504 CAPLUS
DOCUMENT NUMBER: 127:149281
TITLE: Process for the production of finasteride **polymorphic** form I via crystallization
INVENTOR(S): McCauley, James A.; Varsolona, Richard J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 6 pp., Cont.-in-part of U.S. 5,468,860.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5652365	A	19970729	US 1995-411685	19950330
US 5468860	A	19951121	US 1993-10734	19930129
WO 9411387	A2	19940526	WO 1993-US10659	19931105
WO 9411387	A3	19940929		
W: BB, BG, BR, BY, CZ, FI, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PL 179379	B1	20000831	PL 1993-309050	19931105
US 5886184	A	19990323	US 1997-824426	19970326

PRIORITY APPLN. INFO.:

US 1992-978535	B2	19921119
US 1993-10734	A2	19930129
WO 1993-US10659	W	19931105
US 1995-411685	A3	19950330

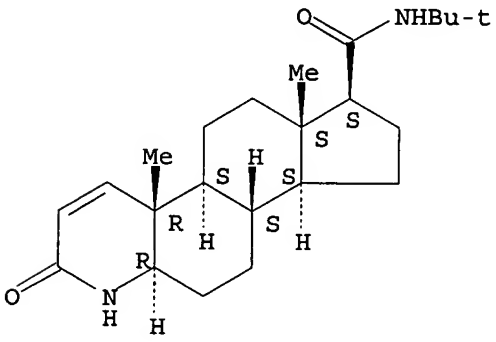
AB **Polymorphic** form I of finasteride, 17β-(N-tert-Bu carbamoyl)-4-aza-5α-androst-1-en-3-one, is produced in substantially pure form using the steps of: (1) crystallization from a solution of finasteride in a water immiscible organic solvent and 0% or more by weight of water, producing solvated and non-solvated finasteride in solution, such that the amount of organic solvent and water in the solution is sufficient to cause the solubility of the non-solvated form of finasteride to be exceeded and the non-solvated form of finasteride to be less soluble than any other form of finasteride in the organic solvent and water solution: (2) recovering the resultant solid phase; and (3) removing the solvent therefrom; wherein the water immiscible organic solvent is Et acetate or iso-Pr acetate and the amount of water in the solvent mixture is below 4 mg./mL.

IT **98319-26-7DP**, Finasteride, **polymorphic** Form I
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystallization of **polymorphic** Form I of finasteride)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:1006742 CAPLUS
DOCUMENT NUMBER: 124:117692
TITLE: New finasteride processes
INVENTOR(S): Dolling, Ulf H.; McCauley, James A.; Varsolona, Richard J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 4 pp. Cont.-in-part of U.S. Ser. No. 978,535, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5468860	A	19951121	US 1993-10734	19930129
WO 9411387	A2	19940526	WO 1993-US10659	19931105
WO 9411387	A3	19940929		

W: BB, BG, BR, BY, CZ, FI, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ
RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

RU 2120445	C1	19981020	RU 1995-112521		19931105
RO 115164	B1	19991130	RO 1995-940		19931105
RO 115165	B1	19991130	RO 1999-785		19931105
CZ 287842	B6	20010214	CZ 1995-1268		19931105
SK 281765	B6	20010710	SK 1995-659		19931105
PL 186740	B1	20040227	PL 1993-333738		19931105
IL 107574	A1	20000716	IL 1993-107574		19931111
IL 125769	A1	20030312	IL 1993-125769		19931111
IL 125770	A1	20040219	IL 1993-125770		19931111
EP 599376	A2	19940601	EP 1993-203163		19931112
EP 599376	A3	19940928			
EP 599376	B1	19980408			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
EP 655458	A2	19950531	EP 1995-200270		19931112
EP 655458	A3	19960710			
EP 655458	B1	19990303			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
EP 823436	A2	19980211	EP 1997-201712		19931112
EP 823436	A3	19981125			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
AT 164850	E	19980415	AT 1993-203163		19931112
ES 2052476	T3	19980616	ES 1993-203163		19931112
AT 177112	E	19990315	AT 1995-200270		19931112
ES 2072848	T3	19990501	ES 1995-200270		19931112
CA 2103107	AA	19940520	CA 1993-2103107		19931115
AU 9350787	A1	19940616	AU 1993-50787		19931118
AU 658774	B2	19950427			
JP 06199889	A2	19940719	JP 1993-289536		19931118
JP 07110875	B4	19951129			
ZA 9308620	A	19940804	ZA 1993-8620		19931118
HU 66973	A2	19950130	HU 1993-3275		19931118
HU 216195	B	19990528			
JP 09235294	A2	19970909	JP 1996-259373		19931118
HR 931410	B1	20000630	HR 1993-931410		19931118
CN 1090583	A	19940810	CN 1993-114530		19931119
CN 1058018	B	20001101			
US 5652365	A	19970729	US 1995-411685		19950330
FI 9502422	A	19950518	FI 1995-2422		19950518
FI 107450	B1	20010815			
NO 9501986	A	19950519	NO 1995-1986		19950519
US 5886184	A	19990323	US 1997-824426		19970326
HK 1008338	A1	20000505	HK 1998-109309		19980721
LV 12212	B	19990320	LV 1998-236		19981026
NO 9900468	A	19950519	NO 1999-468		19990201
NO 307888	B1	20000613			
BG 64464	B1	20050331	BG 1999-103170		19990211
NO 9902580	A	19950519	NO 1999-2580		19990528
NO 307609	B1	20000502			
LV 12460	B	20000920	LV 2000-26		20000223
HR 2000000295	A1	20000831	HR 2000-295		20000512
HR 20000295	B1	20020831			
FI 2001000289	A	20010215	FI 2001-289		20010215
FI 2001000290	A	20010215	FI 2001-290		20010215
FI 114215	B1	20040915			
FI 2004000559	A	20040421	FI 2004-559		20040421
PRIORITY APPLN. INFO.:			US 1992-978535	B2	19921119
			US 1993-10734	A	19930129
			WO 1993-US10659	W	19931105
			IL 1993-107574	A3	19931111
			EP 1993-203163	A3	19931112
			JP 1993-289536	A3	19931118
			US 1995-411685	A3	19950330

OTHER SOURCE(S): CASREACT 124:117692

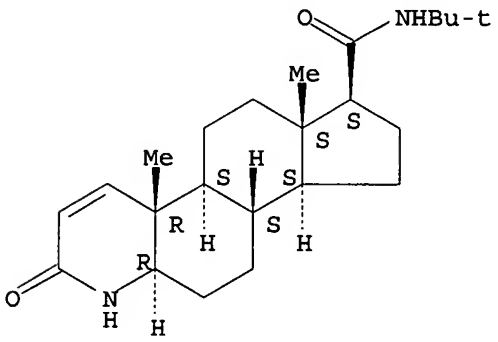
AB Finasteride is prepared by treating a carboxylic ester analog with Me3CNH2 in presence of an organomagnesium halide, present in at least a 2:1 molar ratio to the ester. Two **polymorphic** crystalline forms of finasteride are also prepared Thus, Me 3-oxo-4-aza-5α-androst-1-en-17α-carboxylate was treated with Me3CNH2 and 2 mol of EtMgBr to give 97% finasteride.

IT **98319-26-7P**, Finasteride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of finasteride)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:662923 CAPLUS

DOCUMENT NUMBER: 123:162781

TITLE: Steroid 5α-reductase nucleic acid segments and recombinant vectors and host cells

INVENTOR(S): Andersson, Sefan; Russell, David W.

PATENT ASSIGNEE(S): The University of Texas System, USA

SOURCE: U.S., 72 pp. Cont.-in-part of U.S. Ser. No. 517,661, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5422262	A	19950606	US 1991-795859	19911118
CA 2079454	AA	19911031	CA 1991-2079454	19910425
CA 2079454	C	20020226		
AT 129013	E	19951015	AT 1991-909339	19910425
US 5679521	A	19971021	US 1995-457616	19950601
PRIORITY APPLN. INFO.:			US 1990-517661	B2 19900430
			US 1991-795859	A3 19911118

AB Disclosed are methods and compns. for the preparation of rat and human steroid 5α-reductases by recombinant means, as well as for the use of these enzymes in screening assays for the identification of compds. which have the ability to inhibit or otherwise alter the enzymic function of these enzymes. Biochem. and pharmacol. evidence is presented to demonstrate the existence of more than one human steroid 5α-reductase. The DNA sequence encoding steroid 5α-reductase 2, the major active isoenzyme

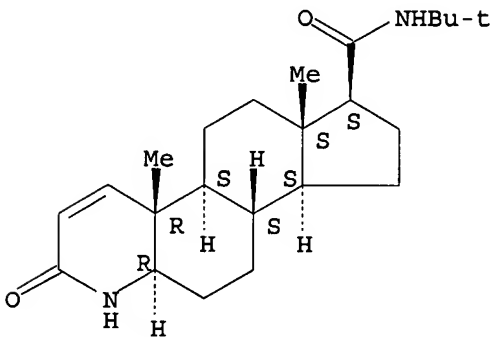
of human genital tissue, is disclosed, in addition to methods and compns. for its preparation and pharmacol. anal. Mutations in the steroid 5α-reductase 2 gene are shown to underlie male pseudohermaphroditism. The sequences disclosed herein may be used directly in the preparation of genetic constructs, or may be employed in the preparation of hybridization probes for the selection of enzyme-encoding sequences from other sources. These sequences may prove useful in an anal. of normal and abnormal sexual differentiation, benign prostatic hyperplasia, male pattern baldness, acne, hirsutism, endometriosis, and cancer of the prostate [no data].

IT **98319-26-7**, Finasteride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(human and rat steroid 5α-reductase nucleic acid segments and recombinant vectors and host cells)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:255357 CAPLUS
DOCUMENT NUMBER: 122:47508
TITLE: Cloning and expression of a cDNA for a human α1C adrenergic receptor for use in screening of ligands for therapeutic use
INVENTOR(S): Bayne, Marvin L.; Clineschmidt, Bradley V.; Strader, Catherine D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421660	A1	19940929	WO 1994-US2609	19940310
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2158345	AA	19940929	CA 1994-2158345	19940310
AU 9464453	A1	19941011	AU 1994-64453	19940310
AU 685789	B2	19980129		

EP 689547	A1	19960103	EP 1994-912209	19940310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08508163	T2	19960903	JP 1994-521115	19940310
PRIORITY APPLN. INFO.:			US 1993-32849	A 19930315
			WO 1994-US2609	W 19940310

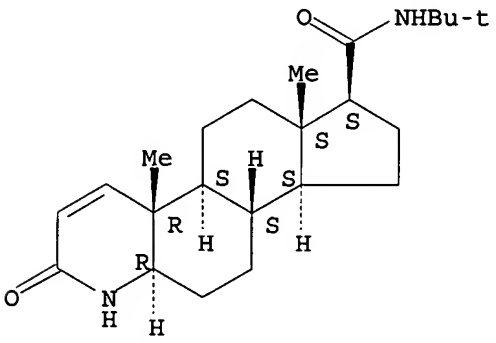
AB A cDNA for a human α1C adrenergic receptor is cloned and used in an in vitro assay to screen for compds. that specifically bind to the receptor, including compds. that reduce symptoms of benign prostatic hypertrophy. Partial cDNAs for the receptor were cloned by PCR using primers derived from conserved peptides from α-adrenergic receptors and these were used to assemble a full-length cDNA. The identity of the clone was confirmed by expression of the cDNA in COS-7 cells using pcDNAI-neo and demonstration of specific binding of [125I]-HEAT. Two alleles of the receptor gene, encoding receptors with somewhat different pharmacologies, were obtained. Methods for screening for ligands of the receptor are described.

IT **98319-26-7**, Finasteride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of, in treatment of benign prostatic hyperplasia; cloning and expression of a cDNA for a human α1C adrenergic receptor for use in screening of ligands for therapeutic use)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

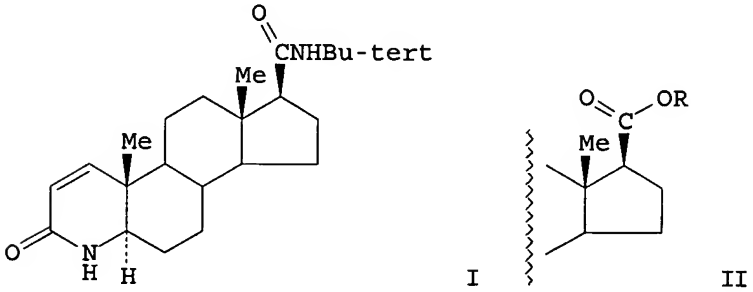


L4 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1994:557962 CAPLUS
DOCUMENT NUMBER:	121:157962
TITLE:	A process for the production of finasteride and its **polymorphs**
INVENTOR(S):	Dolling, Ulf H.; McCauley, James A.; Varsolona, Richard J.
PATENT ASSIGNEE(S):	Merck and Co., Inc., USA
SOURCE:	Eur. Pat. Appl., 11 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 599376	A2	19940601	EP 1993-203163	19931112
EP 599376	A3	19940928		
EP 599376	B1	19980408		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
US 5468860 A 19951121 US 1993-10734 19930129
EP 655458 A2 19950531 EP 1995-200270 19931112
EP 655458 A3 19960710
EP 655458 B1 19990303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
EP 823436 A2 19980211 EP 1997-201712 19931112
EP 823436 A3 19981125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
PRIORITY APPLN. INFO.: US 1992-978535 A 19921119
US 1993-10734 A 19930129
EP 1993-203163 A3 19931112
OTHER SOURCE(S): CASREACT 121:157962; MARPAT 121:157962
GI



I II

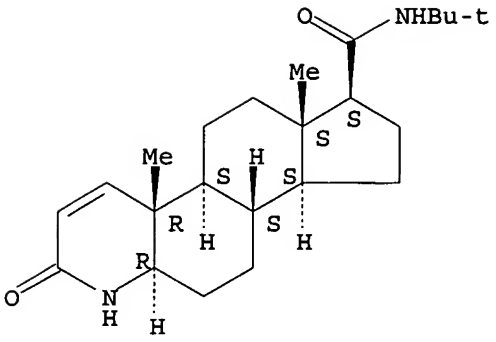
AB The 5α-reductase inhibitor finasteride (I) is prepared by reaction of 17β-carboalkoxy-4-aza-5α-androst-1-en-3-ones II [R = C1-10 linear, branched, or cyclic alkyl with optional Ph substituent(s)], as their Mg halide salts, with t-butylaminomagnesium halide, present in at least a 2:1 molar ratio to II, formed from tert-BuNH2 and an aliphatic/aryl magnesium halide at ambient temperature in an inert organic solvent under an inert atmospheric, followed by heating and recovering I. In 2 examples using II (R = Me), EtMgBr, and tert-BuNH2, under N in refluxing THF (12 h), I was prepared in 97% yield. Also disclosed are 2 **polymorphic** crystalline forms of I, and methods of their production Dissolving I in glacial AcOH and adding H2O up to ≥84 weight% H2O gives form I, whereas adding H2O up to 75-80 weight% H2O gives form II.

IT **98319-26-7P**, Finasteride
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and **polymorphic** forms of)

RN 98319-26-7 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

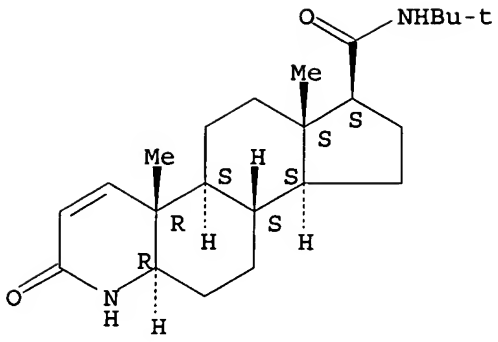


L4 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:168704 CAPLUS
DOCUMENT NUMBER: 116:168704
TITLE: Genetic and pharmacological evidence for more than one human steroid 5α-reductase
AUTHOR(S): Jenkins, Elizabeth P.; Andersson, Stefan; Imperato-McGinley, Julianne; Wilson, Jean D.; Russell, David W.
CORPORATE SOURCE: Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
SOURCE: Journal of Clinical Investigation (1992), 89(1), 293-300
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The enzyme steroid 5α-reductase catalyzes the conversion of testosterone into the more potent androgen, dihydrotestosterone, and impairment of this reaction causes a form of male pseudohermaphroditism in which genetic males differentiate predominantly as phenotypic females. The authors previously isolated several cDNA clones that encode a human steroid 5α-reductase enzyme. Here, mol. and genetic studies are reported demonstrating that the gene encoding this cDNA is normal in subjects with the genetic disease steroid 5α-reductase deficiency. It is also shown that in contrast to the major steroid 5α-reductase in the prostate and cultured skin fibroblasts, the cDNA-encoded enzyme exhibits a neutral to basic pH optima and is much less sensitive to inhibition by the 4-aza steroid, finasteride (MK-906). The results provide genetic, biochem. and pharmacol. support for the existence of at least 2 steroid 5α-reductase isoenzymes in man.

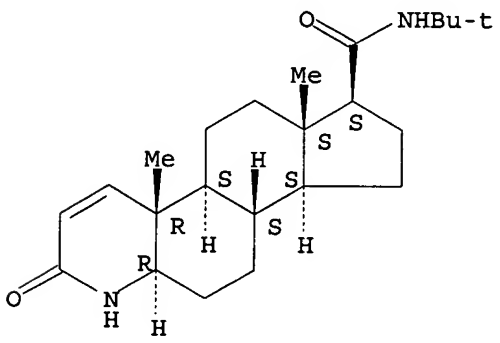
IT **98319-26-7**, Finasteride
RL: BIOL (Biological study)
(steroid reductase isoenzymes of human inhibition by, kinetics of)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:663327 CAPLUS
DOCUMENT NUMBER: 115:263327
TITLE: Detection and characterization of **polymorphism** in the pharmaceutical industry
AUTHOR(S): McCauley, J. A.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: AIChE Symposium Series (1991), 87(284, Part. Des. Cryst.), 58-63
CODEN: ACSSCQ; ISSN: 0065-8812
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Polymorphs** of sulindac, phthalylsulfathiazole, Proscar and ibuprofen lysinate were studied by DTA and x-ray powder diffraction as well as their solubility
IT **98319-26-7**, Proscar
RL: PRP (Properties)
(**polymorphism** of)
RN 98319-26-7 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'REGISTRY' ENTERED AT 14:29:48 ON 09 FEB 2006

10/801,069

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L1             1 S FINASTERIDE/CN

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L2           771 S L1
L3        181229 S POLYMORPH?
L4            18 S L2 AND L3

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L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   98319-26-7  REGISTRY
ED   Entered STN:  29 Sep 1985
CN   1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1,1-dimethylethyl)-
     2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-,
     (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4-Azaandrost-1-ene-17-carboxamide, N-(1,1-dimethylethyl)-3-oxo-,
     (5α,17β)-
OTHER NAMES:
CN   Chibro-Proscar
CN   Finasteride
CN   Finastid
CN   Finpecia
CN   MK 906
CN   Propecia
CN   Proscar
CN   Prostide
FS   STEREOSEARCH
MF   C23 H36 N2 O2
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
       BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, CSNB,
       DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS,
       IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT,
       PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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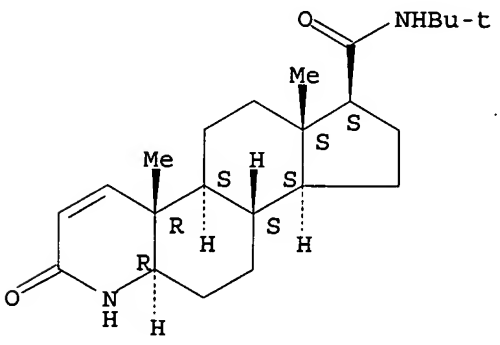
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

767 REFERENCES IN FILE CA (1907 TO DATE)

10/801,069

10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
770 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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